Research Article | Vol. 12, No. 5 / 1 May 2021 / Biomedical Optics Express 2550

Biomedical Optics EXPRESS

Effect of cataract-induced refractive change on intraocular lens power formula predictions

David L. Cooke,[1,2,*] **Timothy L. Cooke,**[1] **and David A. Atchison**[3]

[1] *Great Lakes Eye Care, 2848 Niles Road, Saint Joseph, MI 49085, USA*
[2] *Department of Neurology and Ophthalmology, Michigan State University, College of Osteopathic Medicine, 965 Wilson Rd, East Lansing, MI 48824, USA*
[3] *Centre for Vision and Eye Research, Queensland University of Technology, Kelvin Grove, Q, Australia*
[*] *davidLcooke@gmail.com*

Abstract: Cataract-induced refractive change (*CIRC*) is the change in refraction induced by a cataract. It can amount to several diopters (D). It alters predicted errors in refraction following cataract surgery through changes in axial length measurement. This study determined the effect of *CIRC* on the accuracy of intraocular lens power formula predictions of refraction in 872 eyes of 662 patients. Regression of results gave −0.030 D prediction error per 1 D of *CIRC*, i.e. cataract-induced myopia and hyperopia tended to yield postoperative hyperopia and myopia, respectively. Theoretical determinations with a model eye supported this result. There was significant correlation of nuclear cataract opalescence with *CIRC*. Although these effects are difficult to identify based on changes in refraction, if biometers were able to identify cataract density and automatically adjust axial length measurement, IOL power predictions might improve.

1. Introduction

As cataracts develop, several diopters of refractive change can be induced. We later refer to a patient who gained 16 diopters of myopia over 10 years as her cataract developed. We refer to this as cataract-induced refractive change (*CIRC*). This can be explained by a change in the refractive index of the lens.

Suppose that an eye develops a cataract where the refractive index of the lens is higher than it was before. This has two related effects. The first effect is on the refraction of the eye. When the refractive index of the lens increases, the boundaries of the lens with the aqueous and vitreous have larger refractive index differences. As a result, light beams bend more at the lens boundaries, moving the focal point anterior in the eye: there is a myopic shift in refraction.

The second effect of the higher refractive index of the cataractous lens is on axial length measurement and secondarily on IOL power calculations. Optical biometers measure the length of the eye by measuring the time it takes for light to traverse the eye. When the refractive index of the lens increases, light travel slows through the lens. This causes biometers to measure a greater optical path length than prior to development of the cataract. The assumed lens refractive index used by an optical biometer when converting the optical path length to geometric length is now incorrect, and the axial length of the eye is overestimated. When this artifactually long axial length is used in IOL power formulas, they recommend IOL powers that are too low, which should lead to a hyperopic postoperative "surprise."

If the refractive index of the crystalline lens decreases rather than increases, instead of a myopic shift in refraction, overestimation of eye length and a post-operative hyperopic surprise, there is a hyperopic shift in refraction, underestimation of eye length and a myopic surprise.

Two papers are in line with the arguments presented above; these found that increasing nuclear density caused eyes to be measured too long. Axial length was measured with partial coherence

#422190 https://doi.org/10.1364/BOE.422190
Journal © 2021 Received 10 Feb 2021; revised 15 Mar 2021; accepted 26 Mar 2021; published 2 Apr 2021

Biomedical Optics EXPRESS

interferometry, and cataract density was determined by a slit-lamp grading system [1] and by Scheimpflug camera nuclear density grading [2].

We surmised that because cataract development can create either cataract-induced hyperopia or cataract-induced myopia, the measured axial length of the eye could be too long in some cases and too short in others. Unfortunately, it is rare to observe two preoperative biometry readings several years apart, before and after cataract development because biometry is generally performed only after the cataract has progressed. Similarly, because this was a retrospective study, we did not have post-operative measurements. Lacking this information, we investigated indirectly how *CIRC* is likely to affect biometry measurements.

There are three approaches in this paper:

1. Empirical approach: a) We determined the effect of *CIRC* on intraocular lens (IOL) power formula (post-operative refraction) prediction errors. b) Using IOL power formula calculations, we determined the prediction errors caused by particular axial length errors. Combining the *CIRC*/prediction error and AL error/prediction error relationships allowed us to calculate the effect of *CIRC* on axial length measurements.

2. Theoretical approach: We predicted the effect of *CIRC* on prediction errors using ray-tracing in a model eye.

3. Clinical findings: We related *CIRC* to cataract opalescence obtained with a slit-lamp method.

2. Method

2.1. General

This study conformed to ethics codes based on the tenets of the Declaration of Helsinki. An institutional review board (Lakeland Hospitals Niles and St. Joseph, Institutional Review Board #1) exempted the study from review. This research was compliant with the U.S. Health Insurance Portability and Accountability Act.

2.2. Empirical approach

2.2.1. Determining prediction error from CIRC

Throughout this paper, six different refractions terms are mentioned: 1). Refraction before development of cataract, 2) Refraction after development of cataract, 3) Predicted refraction, 4) Post-operative refraction, 5) Cataract-induced refractive change (*CIRC*) which equals refraction after development of cataract – refraction before development of cataract (2–1), and 6) Prediction error which equals post-operative refraction − predicted refraction (4–3).

We have previously described a dataset of 1454 eyes from 1079 patients obtained at Great Lakes Eye Care [3]. Medical records of patients who underwent small-incision ($\leq$ 3.0 mm-wide surgical wound) phacoemulsification cataract surgery between March 2010 and December 2012 were reviewed. Eyes meeting the following criteria were included initially: complete preoperative data captured from the Lenstar LS900 (Haag-Streit AG, Bern Switzerland), postoperative corrected distance visual acuity of at least 20/25, uncomplicated in-the-bag placement of an AcrySof SN60WF intraocular lens (Alcon laboratories, Inc., Fort Worth, TX), no additional ocular surgery, no history of contact lens wear, and no ocular or systemic disease that might have prevented obtaining good preoperative measurements. No eyes were excluded due to unexpected refractive outcomes.

We selected eyes for which pre-cataractous refractions were known and were between two and fifteen years prior to cataract surgery. This resulted in a dataset of 872 eyes of 662 patients. Our office had performed the prior refraction in 619 eyes. For the other 253 eyes we had access only

Biomedical Optics EXPRESS

to the refraction the patient was wearing. We asked these patients how old their glasses were. Typically, they estimated the age of the glasses in yearly increments once the glasses were at least 2 years old. If so, we arbitrarily assigned July 1 as the day in that year that the patient received the pre-cataract refraction. The age of the pre-cataract refraction was determined by subtracting the date of the pre-cataract refraction from the date of the preoperative visit for cataract extraction.

CIRC was calculated for each eye by subtracting the spherical equivalent of the initial (pre-cataractous visit) refraction from the final (preoperative visit) refraction. A minus *CIRC* value indicates an eye with cataract-induced myopia. Axial length was measured with the Lenstar LS900 biometer.

To limit the effect of any one formula on results of this study, we calculated predicted spherical equivalent refractions using the average of eight IOL formulas for each eye. This average value was used as if there were only one prediction for an eye, not 8 separate predictions. The formulas were Barrett Universal II [4], Haigis [5], Hoffer Q [6–8], Holladay 1 [9], Holladay 2 [10], Olsen [11–13], Sanders-Retzlaff-Kraff/Theoretical [14], and T2 [15]. The Holladay 2 and Olsen formulas were accessed via their respective software. Each IOL formula requires preoperative values such as axial length and keratometry. After entering these values and the IOL power used, each formula gives a predicted refraction. Optimized constants were derived using computer software as previously described [3]. Other calculations were performed with Excel 2010 (version 14.0) and Microsoft SQL Server (version 12.0.2000.8, Microsoft Corp.). Prediction error was defined as the postoperative spherical equivalent refraction minus the predicted refraction.

2.2.2. Determining prediction error from axial length error

Axial lengths measured for each of the 872 eyes prior to surgery were changed by +0.05 to −0.05 mm to simulate the small errors anticipated in axial length measurement. Changes in the average prediction error were determined for each patient. A regression was performed on prediction error change as a function of axial length change.

2.3. Theoretical approach

This approach follows a technique for determining artifacts in eye length measurements during accommodation [16]. We applied ray-tracing, using the well-known Navarro schematic eye, which is representative of four-refracting surface models [17]. It has an axial length of 24.004 mm, lens thickness of 4.0 mm, an optical path length (OPL) of 32.432 mm, and a mean refractive index of 32.432/24.004 = 1.35109. We treated this mean refractive index like the equivalent value described by Haigis in the calibration of the IOLMaster (Carl Zeiss AG, Jena, Germany) axial length to ultrasound axial length [5].

In our model eye, a cataract operation was simulated by replacing the crystalline lens with a thin (i.e. zero thickness) intraocular lens, at a location 5.1 mm inside the eye. We chose this location from analysis of 225 post-operative eyes in our practice. Using biometric measurements with the Lenstar LS900 and the assumption that the second principal planes of IOLs were located two-thirds of the lens thickness into the lens, the distance from the anterior cornea to this location was 5.06 ± 0.28 mm. The model intraocular lens would need +19.296 D power for emmetropia.

We manipulated the crystalline lens refractive index, from the Navarro original value of 1.42, to values between 1.41 and 1.44, such as might be considered to be produced by cataract, to give new preoperative OPLs, new estimated lengths, new refractions (the *CIRC*), intraocular lens powers, and new refractions (the prediction errors). As an example, if the lens refractive index of the Navarro eye lens is increased to 1.43, *OPL* is increased to 32.472 mm, the estimated eye length is 32.472/1.35109 = 24.034 mm which is an artifactual increase in axial length of 0.0296 mm, the ocular refraction or *CIRC* is −1.646 D, the power of the intraocular lens is decreased to +19.185 D power, and there is a prediction error of +0.077 D. Using this ray-tracing method, prediction errors were calculated for various *CIRC* values. The results were plotted as a dashed line in Fig. 1.

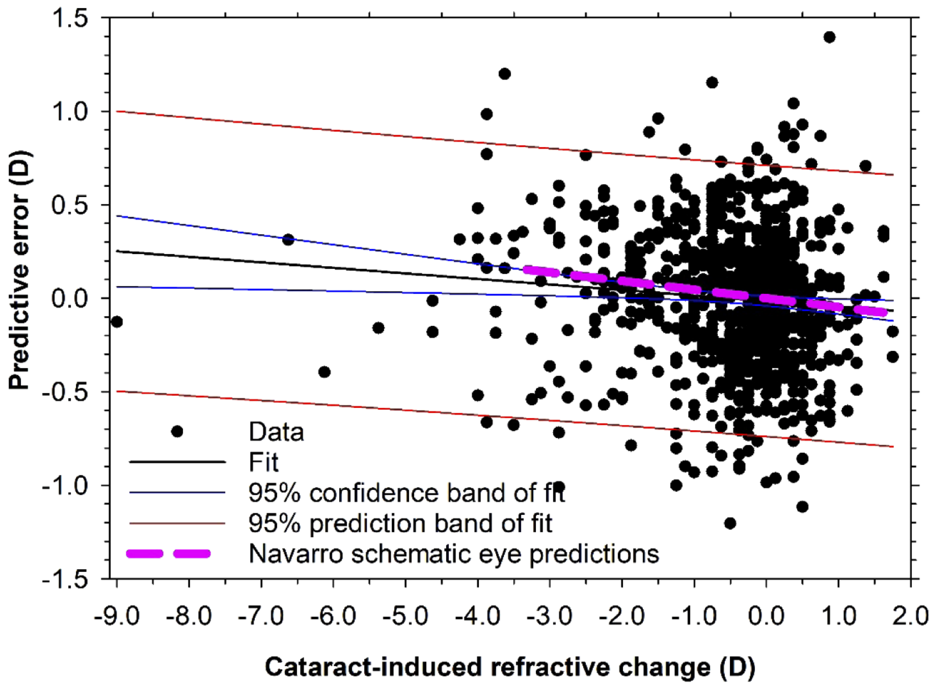

Fig. 1. Prediction error as a function of cataract-induced refractive change. The regression fit is $y = -0.030x\ (\pm 0.022) - 0.015\ (\pm 0.026)$, $R^2 = 0.008$, $p = 0.009$, with bracketed numbers indicating the 95% confidence limits of the slope and y-intercept. The dashed line shows the prediction error on the basis of ray-tracing with the Navarro model eye.

2.3.1. Clinical findings

Great Lakes Eye Care has a standardized cataract grading system. There is a direct crossover to the LOCS III scheme [18] for grades of nuclear opalescence of 4 and above. Nuclear opalescence grades 4, 5, and 6 (NO4-NO6) were identified in our dataset and lower values were categorized as < NO4. Most eyes (n = 697) were categorized as < NO4.

3. Results

3.1. Empirical approach

The length of time between the first, pre-cataract, refractions and the final, pre-operative, refractions averaged 4.4 ± 2.3 years (range 2.0 to 14.9 years). At the preoperative examination, 270 (31%) eyes had more hyperopia than given by the pre-cataractous refraction, 510 (58%) were more myopic, and 92 (11%) were unchanged (difference 0.00 D).

Additional population characteristics include [mean (range)]: axial length [23.83 (20.84 to 29.51) mm]; average keratometry [43.85 (39.20 to 49.54) D]; anterior chamber depth [3.15 (2.07 to 4.23) mm]; lens thickness [4.66 (3.39 to 5.86) mm], and age [72 (38 to 93) years].

Figure 1 shows post-operative refraction prediction error as a function of *CIRC*. *CIRC* ranged from – 9 D to +1.75 D, and prediction errors ranged from −1.2 to +1.5 D. The regression is:

$$\mathit{Prediction\ Error} = -0.030 \times \mathit{CIRC} - 0.015$$

Biomedical Optics EXPRESS

The 95% confidence limits of slope and y-intercept, respectively, were ±0.022 D and ±0.026 D ($R^2 = 0.008$, $p = 0.009$). The slope of the trendline fit of −0.030 means that −0.03 D of prediction error is predicted by each diopter of *CIRC*; while significant, this explains only 0.8% of the variation of the data (contribution in % is $R^2 \times 100$).

From section 2.2.2, the following formula was obtained:

$$\textit{Change in Prediction Error} = 2.339 \times \textit{Axial length change}\ (R^2 = 1.0).$$

Combining the slopes of the two equations indicates that each −1 D *CIRC* corresponds to +0.030 D prediction error and +0.013 mm axial length error.

3.2. Theoretical approach

Figure 1 includes results from our theoretical approach using the Navarro schematic eye data, which has a slope of −0.047. This slope is more negative than −0.030 for the fit data but is closer to the upper 95% confidence interval for the latter. In comparison to the empirical results, each −1D *CIRC* corresponds to +0.047 D prediction error and approximately +0.018 mm axial length error.

3.3. Clinical findings

The data of *CIRC* for each cataract grade failed the assumption of normality, according to the Kolmogorov-Smirnov test, and so the non-parametric, independent samples Kruskal-Wallis test was used. There was significant correlation of nuclear cataract density with *CIRC* (Kruskal-Wallis $H_3 = 94$, $p < 0.001$), with NO4 and NO5 gradings ($p < 0.001$) and NO6 grading ($p = 0.046$) producing significantly more negative *CIRC*s than the < NO4 grading upon pair-wise comparisons with Holm-Bonferroni correction (Fig. 2). According to the LOCS III, nuclear density can be graded as either nuclear color or nuclear opalescence. We used only the latter and found that increased lens opalescence gave more cataract-induced myopia.

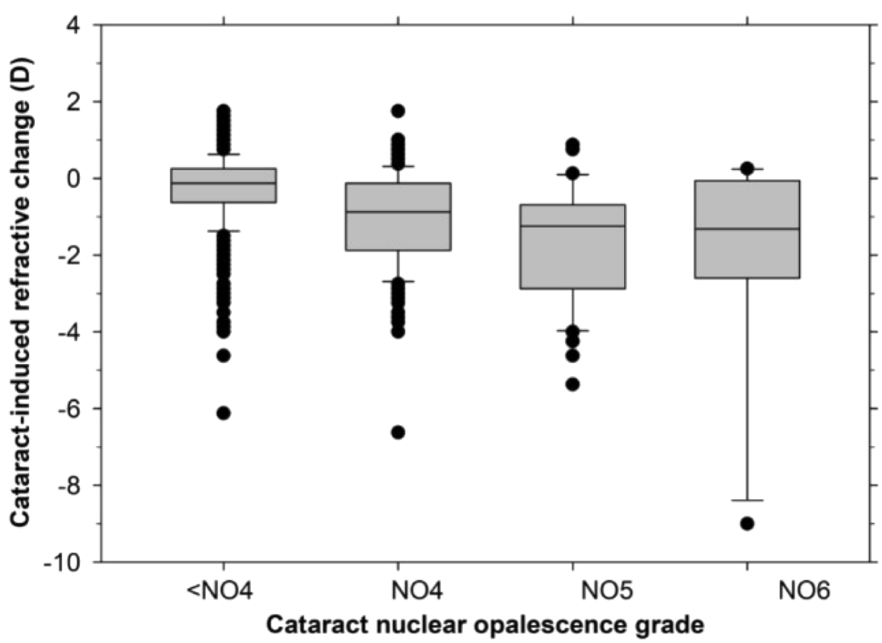

Fig. 2. Box-plot of *CIRC* as a function of lens density classification.

Biomedical Optics EXPRESS

4. Discussion

We have shown that *CIRC* increases prediction error in the direction anticipated – negative (myopic) *CIRC* gives positive (hyperopic) prediction errors; we have also estimated how much axial length error produces that prediction error, and that lens opalescence identifies eyes likely to have become myopic. These results are supported by theoretical ray-tracing. The effect is generally small. Part of the reason it is hard to detect is because refractions are imprecise and we have chosen to show the effect by comparing refractions.

Change in lens refractive index is only one of the factors contributing to *CIRC* and the predictive error. Other contributions to the former can include changes in lens surface curvatures and thickness, while other contributors to the latter include IOL position in the eye, small errors in IOL power and errors in measurements such as corneal power and refraction.

We have noticed that even with the best IOL power calculators, results can still sometimes be very disappointing. A weakness of this paper is that the IOL formula prediction errors created by CIRC are small. However, we believe future improvements will come in small increments as systemic flaws are identified and corrected. The purpose of this current paper is to identify an area for improvement that may enable all formulas to improve.

The theoretical approach was based on uniform refractive index change in the lens. This would affect surface powers, even if the surface shape did not change in cataract. The nature of refractive index change in cataract is not understood, but presumably it involves changes in the gradient index of the lens. In developing myopia, there could be an increase in refractive index in the central part of the lens that increases the rate of change from center to surface, or the change in refractive index change could be more spread out across the lens rather than most of it occurring close to the lens surface [19].

The important aspect of refractive index change in ocular biometry is its effect on the refractive index along the optical axis of the lens, which in turn changes the optical path length of the lens and hence the estimation of actual axial length of the eye. Biometers assume a single refractive index for the axial length, such as the Lenstar LS900 used in this study, or they use pre-set internal refractive indices. There is not an axial length adjustment for subtypes of cataract, such has been identified in ultrasound [20].

Axial length estimation effect from *CIRC* is generally small, but can be considerable in some cases. As an example, a patient was seen in our office at age 31 years for cataract surgery. One eye had no cataract, a manifest refraction of $-1.00 + 1.00 \times 180$ and uncorrected vision of 6/6. By 42 years, a grade 5 nuclear opalescent cataract had developed. Manifest refraction was $-17.00 + 0.75 \times 15$ with corrected vision of 6/18−. Myopic *CIRC* was −16.125 D. Axial length measurement with an IOLMaster v5.4 instrument was 0.2 mm longer at the second than at the first visit. We had no reason to believe the eye had actually lengthened.

Similar to Prinz et al. [1], we were able to find a way at slit lamp to predict an artefactual increase in measured axial length. Prinz et al. graded according to nuclear color by the LOCS III grading system. We found that nuclear opalescence predicted axial length lengthening errors with cataract-induced myopia.

CIRC goes both ways. The range in *CIRC* was from −9.00 D to +1.75 D It is more impressive in the myopic direction, but 30% of our eyes developed hyperopic *CIRC*. There is a possibility that the hyperopic shift might be associated with cortical cataracts, but while there is a clear myopic shift with nuclear cataracts, there is no systematic shift with cortical cataracts [21,22]. Unfortunately, we did not have a slit lamp method to detect eyes with cortical cataracts. In some cases, the eyes with hyperopic shift may be merely showing the same trend that occurs with increasing age to non- or minimally-cataractous eyes [23].

Axial length measurements are likely both too long in some eyes and too short in others due to cataract-induced change in refractive index of the lens. Although the effects were not generally large, they were significant. We hope that digital criteria can be correlated to LOCS III nuclear

Biomedical Optics EXPRESS

opalescence and that biometers will be able to detect such changes and auto-adjust the axial lengths. Such an improvement could increase prediction accuracies of all formulas.

Axial length measurements appear altered by cataract-induced refractive error. If a patient has a large myopic shift from a cataract, one should expect a mildly hyperopic outcome, regardless of the formula used.

Disclosures. The authors declare no conflicts of interest.

References

1. A. Prinz, T. Neumayer, W. Buehl, B. Kiss, S. Sacu, W. Drexler, and O. Findl, "Influence of severity of nuclear cataract on optical biometry," J. Cataract. Refract. Surg. **32**(7), 1161–1165 (2006).
2. T. Ueda, H. Ikeda, T. Ota, T. Matsuura, and Y. Hara, "Relationship between postoperative refractive outcomes and cataract density: multiple regression analysis," J. Cataract Refract. Surg. **36**(5), 806–809 (2010).
3. D. L. Cooke and T. L. Cooke, "Comparison of 9 intraocular lens power calculation formulas," J. Cataract Refract. Surg. **42**(8), 1157–1164 (2016).
4. G. D. Barrett, "Barrett Universal II Formula," Singapore, Asia-Pacific Association of Cataract and Refractive Surgeons, Available at: https://www.apacrs.org/barrett_universal2. Accessed November 12, 2018.
5. W. Haigis, B. Lege, N. Miller, and B. Schneider, "Comparison of immersion ultrasound biometry and partial coherence interferometry for intraocular lens calculation according to Haigis," Graefes Arch. Clin. Exp. Ophthalmol. **238**(9), 765–773 (2000).
6. K. J. Hoffer, "The Hoffer Q formula: a comparison of theoretic and regression formulas," J. Cataract Refract. Surg. **19**(6) 700–712 (1993), errata 20(6), 677 (1994).
7. B. Zuberbuhler and A. J. Morrell, "Errata in printed Hoffer Q formula [letter]," J. Cataract Refract. Surg. **33**(1), 2 (2007), reply by K. J. Hoffer, 2–3.
8. K. J. Hoffer, "Errors in self-programming the Hoffer Q formula," Eye **21**(3), 429 (2007).
9. J. T. Holladay, T. C. Prager, T. Y. Chandler, K. H. Musgrove, J. W. Lewis, and R. S. Ruiz, "A three-part system for refining intraocular lens power calculations," J. Cataract Refract. Surg. **14**(1), 17–24 (1988).
10. J. Holladay, "Holladay IOL Consultant Software & Surgical Outcomes Assessment (version 2014.0607)," Bellaire, TX, Holladay Consulting, 2014 (version 2014.0607).
11. T. Olsen, "IOL Innovations ApS, assignee. System and method for determining and predicting IOL power in situ," US patent 8,657,445 (2014).
12. T. Olsen and P. Hoffmann, "C constant: new concept for ray tracing–assisted intraocular lens power calculation," J. Cataract Refract. Surg. **40**(5), 764–773 (2014).
13. PhacoOptics, Available at https://www.phacooptics.net (version 1.10.100.2020). Accessed June 2, 2019.
14. J. A. Retzlaff, D. R. Sanders, and M. C. Kraff, "Development of the SRK/T intraocular lens implant power calculation formula," J. Cataract Refract. Surg. **16**(3), 333–340 (1990) , erratum, 16(4), 528 (1990).
15. R. M. Sheard, G. T. Smith, and D. L. Cooke, "Improving the prediction accuracy of the SRK/T formula: The T2 formula," J. Cataract Refract. Surg. **36**(11), 1829–1834 (2010).
16. D. A. Atchison and G. Smith, "Possible errors in determining axial length changes during accommodation," Optom. Vis. Sci. **81**(4), 283–286 (2004).
17. R. Navarro, J. Santamaría, and J. Bescós, "Accommodation-dependent model of the human eye with aspherics," J. Opt. Soc. Am. A **2**(8), 1273–1281 (1985).
18. L. T. Chylack, J. K. Wolfe, D. M. Singer, M. C. Leske, M. A. Bullimore, I. L. Bailey, J. Friend, D. McCarthy, and S. Y. Wu, "The Lens Opacities Classification System III. The Longitudinal Study of Cataract Study Group," Arch. Ophthalmol. **111**(6), 831–836 (1993).
19. W. N. Charman and D. A. Adnan Atchison, "Gradients of refractive index in the crystalline lens and transient changes in refraction among patients with diabetes," Biomed. Opt. Express **3**(12), 3033–3042 (2012).
20. D. J. Coleman, F. L. Lizzi, L. A. Franzen, and D. H. Abramson, "Determination of velocity of ultrasound in cataractous lenses," Bibl. Ophthalmol. **83**, 246–251 (1975).
21. K. Pesudovs and D. B. Elliott, "Refractive error changes in cortical, nuclear, and posterior subcapsular cataracts," Br. J. Ophthalmol. **87**(8), 964–967 (2003).
22. M. A. Diez Ajenjo, M. C. Garcia Domene, and C. Peris Martinez, "Refractive changes in nuclear, cortical and posterior subcapsular cataracts: effect of the type and grade," J. Optom. **8**(2), 86–92 (2015).
23. D. A. Atchison and G. Smith, *Optics of the Human Eye*, (Butterworth-Heinemann, 2000), p. 223.